(77%) of crude product. Only a slight loss occurred on recrystallization.

Reaction of I *with HBr* (III). Five g. I was refluxed with 39 ml. 10% HBr for 8 hr. On cooling, the solid which formed was of high apparent purity, and on washing with water and drying it melted sharply at 192–193°. The yield was 5.5 g. (69%).

Anal.: Calcd. for $C_4H_7BrO_3S$: C, 22.3; H, 3.25; Br, 37.2. Found: C, 22.5, 22.3; H, 3.2, 3.2; Br, 37.2, 37.8.

Reaction of III *with $BaCO_3$.* Five and two-tenths g. of the bromohydrin from above was heated for 2 hr. on the steam bath with 2.4 g. $BaCO_3$ in 20 ml. water. The solution became almost completely clear. It was filtered of some residual solid and the filtrate cooled in ice. The solid that formed was recrystallized from ethanol/ethyl acetate; m.p. 158–159°, yield, 2.1 g. (65%). On admixture with Compound I there was no depression of melting point.

Anal.: Calcd. for C_4HO_3S: C, 35.88; H, 4.51; S, 23.89. Found: C, 35.6, 35.9; H, 4.2, 4.3; S, 24.5, 24.41.

Reaction of I *with Ammonia* (V). In 250 ml. of 28% aqueous ammonia was placed 10 g. of I. It was allowed to stand at room temperature for 24 hr. A small amount of a crystalline solid was filtered off that melted (dec.) at 260°. The filtrate was evaporated, and the solid residue triturated with ether, acetone, and ethyl acetate. After drying, it had a m.p. of 198–199°; yield, 7.4 g. (64%).

Anal.: Calcd. for $C_4H_8NO_3S$: C, 31.81; H, 5.92; N, 9.28; S, 21.20. Found: C, 31.9, 31.9; H, 6.3, 6.1; N, 9.4, 9.3; S, 21.4, 21.4.

Acetylation of V (VI). To a mixture of 50 ml. acetic anhydride and 3 ml. acetic acid was added 2.5 g. of V. The mixture was refluxed for 3 hr. The excess anhydride and acid was distilled under vacuum and the residual solid recrystallized from methanol; m.p. 149–150° after drying; yield 3.8 g. (93%).

Anal.: Calcd. for $C_8H_{12}NO_5S$: C, 40.85; H, 5.53; N, 5.95; S, 13.59. Found: C, 40.5, 40.5; H, 5.6, 5.5; N, 5.8, 5.8; S, 13.3, 13.2.

Reaction of II *with acetic anhydride and potassium acetate* (IV). Seventeen g. of II was added to a solution of 10.0 g. KOAc in 200 ml. Ac_2O and 20 ml. HOAc. This mixture was heated on the steam bath overnight, then refluxed 2 hr. further. An inorganic solid was filtered, the filtrate evaporated under vacuum and the solid residue taken up in methanol. Again, some inorganic solid was filtered. The methanol solution was cooled and the crystalline solid recrystallized from methanol. The product weighed 12 g. (68%); m.p. 110–111°.

Anal.: Calcd. for $C_6H_8O_4S$: C, 40.85; H, 4.55; S, 18.18. Found: C, 40.9, 41.1; H, 4.6, 4.67; S, 18.5, 18.7.

Reaction of IV *with ammonia* (V). A mixture of 5.5 g. IV and 90 ml. 28% aq. ammonia was heated on the steam bath for 1 hr. The liquid was distilled under vacuum and the residue recrystallized from ethanol-water after trituration with ethyl acetate; m.p. 197–198°, yield 2.5 g. (48%). Mixed melting point with V from I plus NH_4OH was not depressed.

Reaction of I *with aqueous H_2SO_4* (VII). A solution of 10 g. of I in 50 ml. of 10% H_2SO_4 was refluxed overnight. The acid was neutralized with solid sodium carbonate and the mixture evaporated to dryness. The solid residue was taken up in absolute alcohol, filtered, and the alcohol filtrate cooled. The solid that separated was recrystallized twice from absolute alcohol. After drying it had a m.p. of 159–160°. It depressed the melting point of starting material almost 50° on admixture. It did not depress the m.p. of authentic 3,4-dihydroxytetramethylene sulfone, prepared below.

Dihydroxylation of butadiene sulfone (VII). Butadiene sulfone was dihydroxylated according to the method of Ref. (6) (where 2,5-dihydrothiophene was the starting material) using peracetic acid. The diol VII was the product in 75% yield. It was identical with VII prepared from I by acid hydrolysis (above). The procedure involves finally refluxing the acetic acid solution for 3 hr. to destroy excess peroxide. When I is refluxed in 98% formic acid for 3 hr., it is recovered unchanged.

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Lithium Aluminum Alkoxide Catalyzed Transesterification of Primary Alcohols with Ethyl Acetate

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In the course of another investigation, it was necessary to convert 3-butyl-3-propyloctanoic acid (I) to 3-butyl-3-propyl-1-octanol (II). The reduction was carried out by using an excess of lithium aluminum hydride, followed by destruction of the excess hydride with ethyl acetate, prior to hydrolysis, according to conventional procedures.[1–3]

Upon examining the reaction mixture, it was found that extensive transesterification had taken place, and that a mixture of the expected alcohol (II) and 3-butyl-3-propyl-1-octyl acetate (III) was obtained. Reduction of I to pure II was accomplished successfully by the procedure of Nystrom and Brown[4] by destroying the excess lithium aluminum hydride with dilute sulfuric acid.

As no particular care had been taken to hydrolyze the original reduction mixture immediately after the excess lithium aluminum hydride had been destroyed with the ethyl acetate, it was interesting to examine the reaction system further. A series of reductions of the acid (I) was carried out in which variations were made in the period of time which the reaction mixtures were allowed to stand in contact with a large excess of ethyl acetate before hydrolysis. The mixtures of alcohol (II) and acetate (III) were analyzed by gas chromatography and the results are summarized in Table I. It is noteworthy that even when the reaction mixture was acidified immediately following the introduction of the ethyl acetate, 31% of ester (III) was obtained. The rapidity of the transesterification appeared to be unusual because of the low temperatures involved and the hindered structure of the alcohol (II).

In order to determine if the observed rate of transesterification were peculiar to the structure of the alcohol (II), four reductions of caprylic acid

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(1) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, 1956, p. 1010.

(2) W. G. Brown, *Org. Reactions*, VI, 488 (1951).

(3) R. S. Moffett, *Org. Syntheses*, **33**, 82 (1953).

(4) R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, 69, 1197 (1947).

were performed under comparable conditions with somewhat similar results as is shown in Table I. The relative proportions of *n*-octyl acetate obtained were lower, but still quite significant. In the last experiment shown in the table, only 1.1 g. (0.0125 mole) of ethyl acetate was used in excess, and the product was contaminated by 16% of ester.

TABLE I

TRANSESTERIFICATION OF LITHIUM ALUMINUM HYDRIDE REDUCTION MIXTURES IN THE PRESENCE OF EXCESS ETHYL ACETATE[a]

Acid	Time (hrs.)[b]	% Acetate in Reaction Product	Yield of Acetate, %
I	0	44	31[d]
I	3	71	51[d]
I	24	74	51[d]
n-$C_7H_{15}CO_2H$	0	35	24[d]
n-$C_7H_{15}CO_2H$	3	52	37[d]
n-$C_7H_{15}CO_2H$	16	55	40[d]
n-$C_7H_{15}CO_2H$	3	16[c]	74[e]

[a] The excess lithium aluminum hydride was destroyed with 25 ml. of ethyl acetate. This amounts to a fourfold (.20 mole) excess. [b] Time between addition of ethyl acetate and hydrolysis with 10% sulfuric acid. [c] An excess of only 0.0125 mole of ethyl acetate was employed in this experiment. [d] Per cent yield of ester based on starting acid. [e] Per cent yield of ester based on the ethyl acetate in excess of that required to destroy the excess lithium aluminum hydride.

In Table II are recorded the results of an experiment which was designed to show that ester interchange occurs readily between alkoxides of the type $(RO)_4LiAl$ and ethyl acetate. The preformed alkoxide, $(n\text{-}C_8H_{17}O)_4LiAl$, in ether and an ether solution of ethyl acetate were equilibrated at 29.1°, mixed, samples removed at timed intervals, quenched by addition to dilute acid and worked up. The samples were analyzed by gas chromatography.

TABLE II

REACTION OF $(n\text{-}C_8H_{17}O)_4$LIAL WITH ETHYL ACETATE[a]

Time after Mixing (mins.)	% *n*-Octyl Acetate In mixture	% Yield of *n*-Octyl acetate[b]
1	0.55	2
3	0.66	3
5	0.74	3
10	1.2	5
15	1.3	5
20	1.8	7
30	2.1	8
45	3.1	12
60	3.6	14
120	4.8	19
180	6.5	26

[a] Equimolar amounts of reactants employed. [b] Based on ethyl acetate.

Although the amount of transesterification was less under these conditions, it was still quite significant considering the fact that the ethyl acetate was present in only one-fourth the equivalent quantity required.

The possibility of ester interchange of the lithium aluminum alkoxide of a secondary alcohol with ethyl acetate was considered. When 5-nonanone was reduced with lithium aluminum hydride under conditions similar to those described previously, and the reaction mixture was allowed to stand for 16 hr. with a large excess of ethyl acetate, only the expected carbinol was obtained. Larger highly branched ketones which were reduced previously under essentially the same conditions also gave only carbinols.[5]

EXPERIMENTAL[6]

Materials. Caprylic acid and *n*-octyl alcohol were redistilled Distillation Products Inc. White Label products. Lithium aluminum hydride was purchased from Metal Hydrides, Inc. The 3-butyl-3-propyloctanoic acid (I) was prepared by the method of Rabjohn, Phillips, and DeFeo.[5] 5-Nonanone was obtained by the potassium dichromate oxidation of 5-nonanol.[7]

Reduction of 3-butyl-3-propyloctanoic acid (I). In a 2-l. three necked flask fitted with a condenser protected by a drying tube, a mercury-sealed stirrer, and an addition funnel, were placed 11.4 g. (.30 mole) of lithium aluminum hydride and 500 ml. of dry ether, and the mixture was stirred until a uniform slurry was obtained. A solution of 48.4 g. (.20 mole) of 3-butyl-3-propyloctanoic acid in 150 ml. of dry ether was added dropwise over a period of 2 hr., stirred for an additional 4 hr. and allowed to stand overnight. The excess hydride was destroyed by the dropwise addition of 200 ml. of a 50% solution of ethyl acetate in dry ether. The mixture was hydrolyzed with 500 ml. of 10% sulfuric acid, the layers separated, and the aqueous layer extracted with ether. The combined ether layers were washed with water, 10% sodium bicarbonate solution, again with water, dried over magnesium sulfate, and filtered. The ether was removed at atmospheric pressure and the residue distilled under reduced pressure through a short Vigreux column. There was obtained 47.4 g. of a colorless oil b.p. 115–117.5° (1 mm.), n_D^{25} 1.4448, whose infrared spectrum indicated a mixture of a primary alcohol and an ester.

Separation of the above mixture. In a 500-ml. round-bottomed flask were placed 25.0 g. (.107 mole) of 3,5-dinitrobenzoyl chloride, 42.9 g. of the mixture of alcohol and ester, and 250 ml. of dry pyridine. The mixture was refluxed gently for 2 hr. and allowed to stand overnight. The dark red solution was poured into 400 ml. of 5% sodium hydroxide solution and the resulting mixture was shaken occasionally while standing for 1 hr. The mixture was extracted with ether, the ether extracts washed with water, 10% hydrochloric acid, again with water, 10% sodium bicarbonate solution, again with water, and dried over magnesium sulfate. The solution was filtered, the ether removed at atmospheric pressure, and the residue was distilled under reduced pressure. There was obtained 29.4 g. (68.5%) of III as a colorless oil, b.p. 135–137° (1.5 mm.), n_D^{25} 1.4440.

Anal. Calcd. for $C_{17}H_{34}O_2$: C, 75.50; H, 12.67. Found: C, 75.48; H, 12.39.

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(5) Norman Rabjohn, L. V. Phillips, and R. J. DeFeo, Unpublished results.

(6) All melting points are uncorrected. The carbon-hydrogen analyses were performed by Weiler and Strauss of Oxford, England. The gas chromatographic analyses were performed with the assitance of W. M. Lamkin on a Perkin-Elmer Model 154 Vapor Fractometer.

(7) G. H. Coleman and D. Craig, *Org. Syntheses*, **Coll. Vol. II**, 179 (1943).

The dark, tarry residue from the distillation was extracted with 200 ml. of 95% ethanol, decolorized with carbon, filtered, and concentrated to one-half the original volume. After standing overnight in a refrigerator, there was obtained 22.5 g. (28.4%) of 3-butyl-3-propyl-1-octyl 3,5-dinitrobenzoate (IV) in the form of yellowish crystals, m.p. 42–45°. An analytical sample was obtained from 95% ethanol as fluffy, colorless needles, m.p. 44.5–45°.

Anal. Calcd. for $C_{22}H_{34}O_6N_2$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.60; H, 8.03; N, 6.56.

Saponification of IV. In a 500-ml. three necked flask equipped with a mechanical stirrer and a reflux condenser were placed 20.3 g. (.31 mole) of 85% potassium hydroxide pellets, 200 ml. of 95% ethanol, and 50 ml. of water, and the mixture was stirred until the potassium hydroxide went into solution. To the alkali solution was added 15.4 g. (.037 mole) of IV and the mixture was refluxed for 25 hr. It was allowed to cool and 1-l. of water was added. The mixture was extracted four times with ether, the ether removed, and the residue distilled under reduced pressure. There was obtained 7.1 g. (84.5%) of II as a viscous, colorless oil, b.p. 131–132° (1.5 mm.), n_D^{25} 1.4517.

Anal. Calcd. for $C_{15}H_{32}O$: C, 78.87; H, 14.12. Found: C, 78.85; H, 13.82.

Identification of III. A solution of 20 g. (.30 mole) of 85% potassium hydroxide in 50 ml. of water and 100 ml. of 95% ethanol was refluxed with 10.9 g. of III for 36 hr., cooled, and transferred to a distillation flask. The ethanol was removed by distillation, and after adding 150 ml. of water, the mixture was extracted four times with ether. The combined ether extracts were washed with water, dried over magnesium sulfate, filtered, and the ether removed. The residue was distilled under reduced pressure and 7.8 g. of a colorless, viscous oil, b.p. 139–140° (2.0 mm.), n_D^{25} 1.4519, was obtained whose infrared spectrum was identical with that of 3-butyl-3-propyl-1-octanol (II). Its 3,5-dinitrobenzoate was prepared, m.p. 43–44°, and the melting point was not depressed on admixture with authentic 3-butyl-3-propyl-1-octyl 3,5-dinitrobenzoate (IV).

The aqueous solution was evaporated to dryness and the crude potassium salt was converted to its *p*-bromophenacyl ester, m.p. 84–85°; lit.[8] m.p. 85°.

Preparation of pure II by reduction of I. The reduction of 22.6 g. (.094 mole) of I was acccomplished successfully with 3.8 g. (.10 mole) of lithium aluminum hydride followed by destruction of the excess hydride with 100 ml. of 10% sulfuric acid. After work up, there was obtained 18.4 g. (86.4%) of pure II, b.p. 141–142° (2 mm.), n_D^{25} 1.4520.

Preparation of III from II. A mixture of 8.4 g. (.037 mole) of II, 21.6 g. (.212 mole) of acetic anhydride, 20 ml. of dry thiophene-free benzene, and 2 drops of concentrated sulfuric acid was boiled gently for 3 hr. The solution was cooled, poured into 200 ml. of cold, 10% sodium carbonate solution, and allowed to stand for 2 hr. with occasional stirring. The layers were separated, the aqueous layer extracted with benzene, and the combined benzene solutions washed twice with water. The benzene was removed at atmospheric pressure and the residue distilled under reduced pressure. There was obtained 8.7 g. (87.9%) of III, b.p. 140–142° (2 mm.), n_D^{25} 1.4440, whose infrared spectrum was identical with that of the acetate obtained from the separation of the original reaction mixture.

Anal. Calcd. for $C_{17}H_{34}O_2$: C, 75.50; H, 12.67. Found: C, 75.46; H, 12.92.

Treatment of lithium aluminum hydride reduction mixtures with excess ethyl acetate. The reductions listed in Table I were all carried out in the following manner: A solution of .10 mole of the appropriate acid in 100 ml. of dry ether was added dropwise to a slurry of 3.8 g. (.10 mole) of lithium aluminum hydride in 75 ml. of dry ether, and the mixture was refluxed gently for 3 hr. after addition was complete. It was cooled in an ice bath and 50 ml. of a 50% solution of ethyl acetate in ether was added as rapidly as possible, and the mixture allowed to stand for the indicated time. The complex was hydrolyzed by addition of 100 ml. of 10% sulfuric acid and the mixture was worked up and distilled through a short Vigreux column. In the last run a total of 3.3 g. (.0375 mole) of ethyl acetate in 10 ml. of ether was added, this corresponds to an excess of .0125 mole over that required for destruction of the excess hydride. The mixtures obtained after distillation were analyzed by gas chromatography.

Transesterification of ethyl acetate by $(C_8H_{17}O)_4LiAl$. In a 500-ml. three necked flask fitted with a mercury-sealed stirrer, a condenser protected by a drying tube, and a dropping funnel, were placed 0.95 g. (.025 mole) of lithium aluminum hydride and 50 ml. of dry ether, and the mixture was stirred vigorously for 30 minutes. The flask was placed in a constant temperature bath held at 29.1 ± .05°, and 15 g. (.115 mole) of *n*-octyl alcohol in 75 ml. of dry ether added and the mixture was stirred for an additional 2 hr. to insure temperature equilibrium. A solution of 2.2 g. (.025 mole) of ethyl acetate in 10 ml. of dry ether, which had been equilibrated for 2 hr. in the constant temperature bath, was added in one portion. At timed intervals, 5 ml. portions were pipetted from the reaction mixture, quenched with 10 ml. of cold 10% sulfuric acid, and worked up in the usual fashion. Each sample was analyzed by gas chromatography, and the results obtained are given in Table II.

Reduction of 5-nonanone. The reduction of 28.4 g. (.20 mole) of 5-nonanone in 200 ml. of dry ether was carried out using 5.7 g. (.15 mole) of lithium aluminum hydride in 125 ml. of dry ether. The excess hydride was destroyed with 100 ml. of 50% ethyl acetate in ether, the mixture was allowed to stand for 16 hr., and then was hydrolyzed with 150 ml. of 10% sulfuric acid. After work up, there was obtained 23.7 g. (82.3%) of 5-nonanol, b.p. 90–92° (20 mm.), n_D^{25} 1.4360, whose infrared spectrum showed no traces of carbonyl adsorption.

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[8] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., J. Wiley and Sons, Inc., New York, 1956, p. 276.

Non-lability of the α-Hydrogen during Ninhydrin Oxidation of Alanine[1]

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Recent studies of the reactions of recoil tritium with L(+)-alanine required a degradation method which would remove tritium radioactivity from the α-hydrogen position without affecting any radioactivity in the β-positions.[2] An examination of the proposed mechanism for the oxidation of α-amino acids by ninhydrin showed the original condensation reaction (1), followed by enolization (2) and subsequent hydrolysis (3):[3]

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[1] Research supported by A.E.C. Contract No. AT-(11-1)-407.

[2] J. G. Kay, R. P. Malsan, and F. S. Rowland, *J. Am. Chem. Soc. in press.*

[3] A. Schönberg and R. Moubasher, *Chem. Revs.*, **50**, 261 (1952). R. Moubasher and M. Ibrahim, *J. Chem. Soc.*, 702 (1949). A. Schönberg, R. Moubasher, and A. Mostafa, *J. Chem. Soc.*, 176 (1948). F. G. Baddar, *J. Chem. Soc.*, *S*, 163 (1949).